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REMARKS

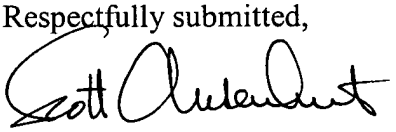
I. Status of the Claims

Claims 1-49 are currently pending. Upon entry of this amendment, claims 21-38 and 44-49 are elected for further prosecution. Claims 21-28, 31-36, 38 and 44-49 are amended without prejudice or disclaimer. These claims are not amended for reasons of patentability. Instead, the claims are amended to conform the claims to the elected subject matter, i.e., methods involving administration of rhesus CMV IL-10 instead of human CMV IL-10. Claims are also amended to correct typographical errors and for increased clarity and consistency in term usage. Also upon entry of this amendment, new claims 50-61 are introduced.

The amended and new claims find support throughout the specification including, for example, at page 9, paragraph 46, and page 24, paragraph 129 to page 26, paragraph 134. Claims 54-55 and 60-61 are also supported at page 15, paragraph 72.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

The title has been replaced as follows:

IMMUNOLOGIC ACTIVITIES
OF RHESUS CYTOMEGALOVIRUS ENCODED IL-10
~~AND HUMAN CYTOMEGALOVIRUS ENCODED IL-10~~

IN THE SPECIFICATION:

Paragraph 48 has been amended as follows:

As used herein, "rhesus cytomegalovirus interleukin 10" or "rhesus CMV IL-10" is defined as a protein which has an amino acid sequence having substantial identity to a known sequence of rhesus CMV IL-10 as described in Lockridge *et al.*, *Virology* (2000) 268:272-280, which is incorporated herein by reference. For the purposes of this invention, some methods ~~used~~ use glycosylated (*e.g.*, produced in eukaryotic cells such as yeast or CHO cells) rhesus CMV IL-10 and some methods ~~used~~ use unglycosylated (*e.g.*, chemically synthesized or produced in prokaryotic cells, such as *E. coli*) rhesus CMV IL-10.

Paragraph 49 has been amended as follows:

As used herein, "human cytomegalovirus interleukin 10" or "human CMV IL-10" is defined as a protein which has an amino acid sequence having substantial identity to a known sequence of human CMV IL-10 as discussed in Kotenko *et al.*, *PNAS* (2000) 97(4):1695-1700, which is incorporated herein by reference. For the purposes of this invention, some methods ~~used~~ use glycosylated (*e.g.*, produced in eukaryotic cells such as yeast or CHO cells) human CMV IL-10 and some methods ~~used~~ use unglycosylated (*e.g.*, chemically synthesized or produced in prokaryotic cells such as *E. coli*) human CMV IL-10.

Paragraph 67 has been amended as follows:

Rhesus and human CMV IL-10 can be used in a number of *in vitro* or *ex vivo* methods. In some methods, cellular responses to these agents are analyzed to provide

information to optimize dosage regimes of these agents *in vivo*. In ~~some, methods~~ some methods, rhesus and human CMV IL-10 are used as positive controls to screen other drugs for effects on lymphocyte proliferation. If the positive control inhibits proliferation of the lymphocytes, whereas a candidate drug does not in a parallel reaction, then it can be concluded that the test drug is ineffective. In other methods, rhesus and human CMV IL-10 are used as research reagents to inhibit proliferation of cells and thereby analyze underlying cellular processes associated with cellular physiology. In other methods, proliferating PBMCs are obtained from a patient with an immune disorder. The lymphocytes are treated with rhesus CMV IL-10 or human CMV IL-10 ex vivo and then returned to the patients.

Paragraph 70 has been amended as follows:

Immune disorders preventable or treatable by methods of the invention include, but are not limited to, the following.

Paragraph 82 has been amended as follows:

Defects in the functioning of the cell-mediated immune response have been implicated in various ~~cell-mediate~~ cell-mediated cytotoxicity immune diseases, such as ~~graft-verses-host~~ graft-versus-host disease. Cytotoxic T lymphocytes (CTLs) are generated by the activation of T cytotoxic (T_c) cells. CTLs have lytic capability and are critical in the recognition and elimination of altered self-cells (*e.g.*, virus-infected cells and tumors). Cytotoxic T lymphocytes (CTLs) are generally $CD8^+$ are therefore class I MHC restricted. Since virtually all nucleated mammalian cells express class I MHC molecules, CTLs can recognize and eliminate almost any altered mammalian cell. This ability of CTLs to recognize and eliminate almost any altered mammalian cell can result in cell-mediated cytotoxicity related immune diseases. Consequently, a decrease in cell surface expression of class I MHC molecules is expected to ameliorate or prevent cell-mediated cytotoxicity related diseases. Thus, decreasing cell surface expression of class I MHC molecules in a patient suffering from a cell-mediated cytotoxicity immune disease by administering an effective dosage of rhesus CMV IL-10 or human CMV IL-10 would be beneficial.

Paragraphs 83 and 84 have been amended as follows:

1. ~~Graft-Verses-Host~~ Graft-versus-Host Disease

~~Graft-verses-host~~ Graft-versus-host disease (GVHD) occurs as a result of *in vivo* cell-mediated cytotoxicity. The disease develops when immunocompetent lymphocytes are introduced into an allogeneic recipient whose immune system is compromised. The grafted lymphocytes begin to attack the recipient and the recipient's compromised state prevents an immune response against the graft. The grafted lymphocytes are carried to the spleen, where they begin to proliferate in response to the allogenetic MHC antigens of the recipient. This proliferation induces an influx of recipient cells to the spleen and results in splenomegaly. The intensity of GVHD can be quantitated by calculating the spleen index (SI). A spleen index of 1.3 or greater is considered to be indicative of GVHD. Enlargement of the spleen is a result of proliferation of both $CD4^+$ and $CD8^+$ T-cell populations.

Paragraph 94 has been amended as follows:

DTH plays an important role in host defense against intracellular pathogens. A variety of pathogens and contact antibodies can induce a DTH response. The initial immune response is nonspecific and often results in significant damage to healthy tissue. Although healthy tissue can be damaged, the patient can successfully eliminate cells infected by intracellular pathogens. When this defense process is not entirely effective, the continued presence of the pathogen's antigens can provoke a chronic DTH reaction. The chronic DTH reaction is characterized by excessive numbers of macrophages and the continued release of lytic enzymes resulting in tissue destruction. Thus, the DTH response to an intracellular pathogen can cause such extensive tissue damage that the DTH response is a pathologic condition. The granulomatous skin lesion seen with *Mycobacterium leprae* and the lung cavitation seen with *Mycobacterium tuberculosis* infections are examples of such pathology resulting from a chronic DTH reaction. Chronic DTH responses can result in granulomatous disease.

Paragraph 285 has been amended as follows:

PENDING CLAIMS

1-20. Non-Elected.

21. (Once amended) A therapeutic or prophylactic method for treating an immune disorder, comprising:

administering to a patient suffering from or susceptible to the immune disorder a pharmaceutically acceptable dose of rhesus CMV IL-10.

22. (Once amended) The method of claim 21, wherein the rhesus CMV IL-10 is a component of a pharmaceutical composition further comprising a pharmaceutically acceptable carrier.

23. (Once amended) The method of claim 22, wherein the pharmaceutical composition is sterile, substantially isotonic and prepared under GMP conditions.

24. (Once amended) The method of claim 21, wherein the immune disorder is selected from the group consisting of graft-versus-host disease, an autoimmune disease, an inflammatory response, a pathologic delayed type hypersensitivity response, endotoxin-induced toxic shock, granulomatis disease, psoriasis, uveitis, systemic lupus erythematous, multiple sclerosis and contact-dermatitis.

25. (Once amended) The method of claim 50, further comprising monitoring proliferation of lymphocytes in the patient to detect a reduction in the level of lymphocyte proliferation responsive to the administering step.

26. (Once amended) The method of claim 21, further comprising monitoring a symptom of the patient to detect amelioration of the symptom responsive to the administering step.

27. (Once amended) The method of claim 21, wherein the patient is suffering from the disorder and the method is a therapeutic treatment method.

28. (Once amended) The method of claim 21, wherein the patient is susceptible to the disorder and the method is a prophylactic treatment method.

29. The method of claim 28, wherein the patient is an organ transplant patient.

30. The method of claim 29, wherein the organ is a kidney.

31. (Once amended) The method of claim 30, wherein IFN-α levels of the patient are detectably decreased responsive to the administering of rhesus CMV IL-10.

32. (Once amended) The method of claim 21, wherein the immune disorder is a chronic inflammatory disease.

33. (Once amended) The method of claim 32, wherein the chronic inflammatory disease is selected from the group consisting of rheumatoid arthritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, Graves' disease, Hashimoto's thyroiditis, systemic lupus erythematosus, multiple sclerosis, scleroderma, and insulin-dependent diabetes mellitus.

34. (Once amended) The method of claim 21, wherein the immune disorder is an allergic response.

35. (Once amended) The method of claim 34, wherein the immune disorder is asthma.

36. (Once amended) The method of claim 21, wherein the patient is suffering from a type TH1 immune response to a transplanted graft.

37. The method of claim 36, wherein the transplanted graft is an organ selected from the group consisting of cornea, lung, heart, liver, bone marrow, kidney, pancreas, blood, and skin.

38. (Once amended) The method of claim 25, wherein the immune disorder is leukemia.

39-43. Non-elected.

44. (Once amended) A therapeutic or prophylactic method for treating an inflammatory response, comprising administering to a patient suffering from or susceptible to the inflammatory response a pharmaceutically acceptable dose of rhesus CMV IL-10.

45. (Once amended) The method of claim 44, further comprising monitoring proliferation of leukocytes in the patient to detect a reduction in the level of leukocyte proliferation responsive to the administering step.

46. (Once amended) The method of claim 44, further comprising monitoring a symptom of the patient to detect amelioration of the symptom responsive to the administering step.

47. (Once amended) The method of claim 44, wherein the patient is suffering from the disorder and the method is a therapeutic method.

48. (Once amended) The method of claim 44, wherein the inflammatory response is a chronic inflammatory disease.

49. (Once amended) The method of claim 48, wherein the chronic inflammatory disease is selected from the group consisting of rheumatoid arthritis, Crohn's disease, ulcerative colitis, Graves' disease, Hashimoto's thyroiditis and insulin-dependent diabetes mellitus.

50. (New) The method of claim 21, wherein the patient is a human.

51. (New) The method of claim 21, wherein the pharmaceutically acceptable dose is administered as a single dose.

52. (New) The method of claim 21, wherein the pharmaceutically acceptable dose is administered as part of a multi-dose regime.

53. (New) The method of claim 50, wherein rhesus CMV IL-10 is administered in an amount sufficient to inhibit proliferation of lymphocytes in the human patient.

54. (New) The method of claim 50, wherein rhesus CMV IL-10 is administered in an amount sufficient to inhibit proliferation of peripheral blood mononuclear cells in the peripheral blood of the human patient.

55. (New) The method of claim 50, wherein rhesus CMV IL-10 is administered in an amount sufficient to inhibit cytokine production in the human patient.

56. (New) The method of claim 44, wherein the patient is susceptible to the inflammatory response and the method is a prophylactic treatment method.

57. (New) The method of claim 44, wherein the patient is a human.

58. (New) The method of claim 44, wherein the pharmaceutically acceptable dose is administered as a single dose.

59. (New) The method of claim 44, wherein the pharmaceutically acceptable dose is administered as part of a multi-dose regime.

60. (New) The method of claim 57, wherein rhesus CMV IL-10 is administered in an amount sufficient to inhibit proliferation of peripheral blood mononuclear cells in the peripheral blood of the human patient.

61. (New) The method of claim 57, wherein rhesus CMV IL-10 is administered in an amount sufficient to inhibit cytokine production in the human patient.